REMARKS

In response to the Office Action dated April 1, 2003, claim 43 has been amended. Claim 43 has been amended to correct the dependency from claim 1 to claim 28. The wrong independent claim was inadvertently recited. Support for the amendment can be found on page 17, lines 5-20. Claim 43 is further clarified. The clarification does not in any way change the scope of the claim. No new matter has been added.

New claim 44 has been added to include other methods of association between the growth factor and the substrate in addition to using an adhesive. Support for the claim can be found throughout the specification, for example on page 6, lines 15-16 and page 13, line 28, to page 20, line 25. No new matter has been added.

Claims 1, 3-4, 8-10, 13-15, 28-29 and 33-43 are pending in the case. Reconsideration of the claims is respectfully requested.

I. Rejection under 35 U.S.C. §112

On page 2 of the Office Action, claim 43 is rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

Applicants have amended claim 43 to correct an inadvertent error in its dependency. Applicants believe that the correction obviates the rejection, and the clarification phrase does not change the scope of the claim in any way. Reconsideration is respectfully requested.

II. Allowability of claims

Applicants thank the Examiner for favorable consideration and allowance of claims 28, 29, and 33. Applicants also thank the Examiner for indicating the allowability of claim 42.

Since claim 43 is dependent from allowed claim 28, claim 43 should also be allowable. Reconsideration is respectfully requested.

III. Rejection under the judicially created doctrine of obvious-type double patenting

On page 3 of the Office Action, claims 1, 3, 4, 8-10, 13-15, 34-40, and 43 were rejected under the judicially created doctrine of obvious-type double patenting as being unpatentable over claims 1, 2, 4-11, 14, 15, and 21-29 of copending Application No. 09/014,087.

Applicants submit that the claims of the present application are distinct and independently patentable from the claims of copending Application Number 09/014,087. Reconsideration is respectfully requested. Additionally, Applicants will consider filing a terminal disclaimer complying with 37 CFR 3.73(b) when these claims are allowed.

IV. Rejection under 35 U.S.C. §102

1. On page 3 of the Office Action, claims 1, 3, 4, 8, 9, and 43 are rejected under 35 U.S.C. §102 (b) as being anticipated by Cahalan, et al. (U.S. 5,308,641).

Applicants respectfully traverse the rejection.

The Cahalan, et al. patent teaches the use of a spacer which presents a stable platform for the attachment of the biomolecule. See col. 2, lines 63-66. The spacer is strongly attached to the material surface. See col. 2, lines 67-68. The polyalkylimine and crosslinking agent together form the spacer used for improving the biocompatability of the substrate to enable the attachment of any biologically active compound to the substrate through the spacer. See col. 4, lines 14-19. Cahalan, et al. stresses that the spacer material intervenes between the substrate and the biologically active compound, and sometimes, a second spacer is used. See col. 4, lines 62-66, and col. 5, lines 44-55. Cahalan, et al. further notes that the light crosslinking of polyalkylimine to the substrate and the light crosslinking in the interface between polyalkylimine and the biomolecule to attach the biomolecule to the polyalkylimine is necessary to prevent the biomolecule from being buried in the spacer and losing bioactivity (col. 3, lines 2-20).

The Examiner's characterization that col. 2, line 66 to col. 3, line 3 of Cahalan, et al. teaches the crosslinking agent crosslinks the surface and provides aldehyde functionality to the surface to bind biomolecules misses the point that the crosslinker and the polyalkylimine formed a spacer and that the spacer intervenes between the substrate and the biological molecule. See col. 4, lines 14-19, and lines 58-66, and col. 5, lines 44-55. This is in contrast to claim 1 of the present invention which teaches association with or direct crosslinking of a growth factor to a substrate without a spacer material.

To anticipate a claim, the reference must teach every element of the claim. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). "The identical

invention must be shown in as complete detail as is contained in the ... claim." *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). Therefore, all claim elements, and their limitations, must be found in the prior art reference to maintain a rejection based on 35 U.S.C. §102. Applicants respectfully submit that Cahalan, et al. fail to teach either the association with or direct crosslinking of a growth factor to a substrate without a spacer material, the subject matter of claim 1. Cahalan, et al. also fails to teach associating growth factors with the substrate by antibody-antigen associations, by specific binding protein-receptor associations or by enzyme-substrate associations, to stimulate association of viable cells with the substrate. Therefore, Cahalan, et al. does not teach every element of claim 1, and therefore fails to anticipate the claims. In addition, Cahalan, et al. specifically teaches away from the association with or direct crosslinking of claim 1.

Dependent claims 3, 4, 8, and 9, which are dependent from independent claim 1, were also rejected under 35 U.S.C. §102(b) as being unpatentable over Cahalan, et al. While Applicants do not acquiesce with the particular rejections to these dependent claims, it is believed that these rejections are moot in view of the remarks made in connection with independent claim 1. These dependent claims include all of the limitations of the base claim and any intervening claims, and recite additional features which further distinguish these claims from the cited references. Therefore, dependent claims 3, 4, 8, and 9 are also in condition for allowance. Applicants respectfully request that the rejection of claims 1, 3, 4, 8, and 9 under 35 U.S.C. §102 be withdrawn.

As for claim 43, Applicants submit that it is dependent from an allowed claim and should also be allowable. Reconsideration is respectfully requested.

2. On page 5 of the Office Action, claim 41 is rejected under 35 U.S.C. §102 (a) as being anticipated by Sharp, et al. (WO 98/00695). The Examiner asserts that the body of claim 41 does not require the preamble for completeness such that the Tat protein bound to a test substrate reads on the claim language. The Examiner further asserts that the Tat protein-to-substrate binding would inherently be done with an enzyme-substrate association because enzymes are proteins as are Tat proteins, and would have inherently had to be bound in the same way to a substrate (page 17, lines 28, et seq.)

Applicants respectfully traverse the rejection.

Sharp, et al. discloses the identification, purification and isolation of proteins, Tat-Stimulatory Factor proteins. See page 3, lines 19-22. Further, it discloses the discovery and identification of kinases that bind the Tat-Stimulatory Factor proteins. See page 3, lines 23-25. However, there is no disclosure or teaching in Sharp, et al. that the Tat-Stimulatory Factor protein is associated with the substrate, effective to stimulate the association of viable cells with the substrate. The substrate-bound Tat-Stimulatory Factor protein is mainly used to bind the kinases, the natural binding partner for Tat-Stimulatory Factor protein, so that the kinases may be isolated. The Tat- Stimulatory Factor protein is used as the substrate in such isolation. See page 17, line 30 to page 18, line 4.

On the other hand, claim 41 is directed to a substrate, and a polypeptide growth factor comprising a Tat protein effective to stimulate the association of viable cells with the substrate.

To anticipate a claim, the reference must teach every element of the claim. Therefore, all claim elements, and their limitations, must be found in the prior art reference to maintain a rejection based on 35 U.S.C. §102. Applicants respectfully submit that Sharp does not teach every element of claim 41, and therefore fails to anticipate claim 41.

IV. Rejection based on 35 U.S.C. § 103(a)

1. On page 4 of the Office Action, claims 10 and 15 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Cahalan, et al. in view of Goldstein (U.S. 5,613,982). The Examiner asserts that Cahalan. et al. discloses medical devices/implants where the crosslinking agent glutaraldehyde attaches the growth factor biomolecule to the substrate-spacer, and that Cahalan, et al.'s solid surface can be made of human or animal tissues, but admits that Cahalan, et al. lacks the type of tissues claimed. However, Examiner then asserts that Goldstein teaches that it was known to make similar medical devices/implants out of heart valves, pericardial tissue and the like (see the whole document and col. 3, lines 14-24), and thus it would have been obvious to use heart valve or pericardial tissue for Cahalan, et al.'s solid surface.

Applicants respectfully traverse the rejection.

Cahalan, et al. teaches attachment of a biomolecule to the spacer which is lightly crosslinked to the substrate using a crosslinking agent. Thus, Cahalan, et al. not only fails to teach association with or direct crosslinking of a growth factor to a substrate without a spacer material, it teaches away from such association or direct crosslinking. The solid surface of Cahalan, et al. is not the substrate, but the spacer. At the same

time, Goldstein teaches a method of preparing a xenogeneic tissue matrix by removing native cells and other antigens from the tissue matrix. See col. 2, lines 44-63. In addition, though Goldstein teaches the generating of bioprosthetic xenografts suitable for human implantation, and mentioned heart valve tissues of porcine or bovine origin (col.3, lines 14-24), it mainly teaches that various enzymatic and chemical treatments to remove viable native cells from implant tissues and organs may be used. See col. 5, lines 12-19. Therefore, Goldstein also fails to teach association with or direct crosslinking of a growth factor to a substrate to stimulate the association of viable cells with the substrate.

Claim 1 of the present invention teaches association with or direct crosslinking of a growth factor to a substrate without a spacer material. This deficiency is found in both Cahalan, et al. and Goldstein.

Claims 10 and 15 are dependent from claim 1. While Applicants do not acquiesce with the particular rejections to these dependent claims, it is believed that these rejections are moot in view of the remarks made in connection with independent claim 1. These dependent claims include all of the limitations of claim 1 and any intervening claims.

Three criteria must be met to establish a *prima facie* case of obviousness. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference. Second, there must be a reasonable expectation of success. Finally, the prior art reference, or combination of references, must teach or suggest all the claim limitations. MPEP § 2142. Since Cahalan, et al. teaches away from association with or direct crosslinking of a biologically active compound to a substrate, and Goldstein also

fails to teach such association with or direct crosslinking of a growth factor to a substrate, the deficiency in Cahalan is therefore not supplied by Goldstein. Applicants respectfully traverse the rejection since the prior art fails to disclose all the claim limitations and there would be no motivation to combine the references as proposed by the Examiner. Claims 10 and 15 are therefore allowable over Cahalan, et al., in view of Goldstein.

2. On page 5 of the Office Action, claim 13 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Cahalan, et al. in view of Bayne, et al. (EP 0 476 983). The Examiner admits that Cahalan, et al. fails to teach VEGF, but believes that Bayne, et al. teaches that it is known to use VEGF as a growth factor. Thus, the Examiner asserts that it would have been obvious to an ordinary artisan to use VEGF as the growth factor of Cahalan.

Applicants respectfully traverse the rejection.

The deficiency of Cahalan, et al., as discussed above, is also applicable here. Bayne, et al. teaches a vascular endothelial cell growth factor isolated and purified from glioma cell conditioned medium. See page 3, lines 46-55. The main focus of Bayne, et al. is on the isolation and characterization of VEGF II mammalian glioma cells. See examples. Thus, Bayne, et al. also fails to teach association with or direct crosslinking of a growth factor to a substrate. See page 8, lines 20-23. The deficiency in Cahalan, et al. is thus not supplied by Bayne, et al. and there is no motivation in Cahalan, et al. to combine with Bayne, et al. to arrive at the present invention. Applicants respectfully submit that since the prior art fails to disclose all the claim limitations of claim 1 and there would be no motivation to combine the references as proposed by the Examiner, this rejection is traversed.

Claim 13 is dependent from claim 1. While Applicants do not acquiesce with the particular rejections to these dependent claims, it is believed that these rejections are moot in view of the remarks made in connection with independent 1. Dependent claim 13 includes all of the limitations of the base claim and any intervening claims, and recite additional features which further distinguish it from the cited references. Therefore, dependent claim 13 is in condition for allowance

3. On page 5 of the Office Action, claim 41 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Sharp, et al. The Examiner notes that one could take the position that the binding of the Tat protein to the substrate is not an enzyme-substrate association. However, the Examiner also asserts that it would have been a matter of obvious design choice to bind the Tat protein to the substrate with an enzyme-substrate association because Applicants have not disclosed that it would provide some advantage, is used for a particular purpose or solves a stated problem.

Applicants respectfully traverse the rejection.

As noted before, Sharp, et al. discloses the identification, purification and isolation of proteins, Tat-Stimulatory Factor proteins. See page 3, lines 19-22. Further, it discloses the discovery and identification of kinases that bind the Tat-Stimulatory Factor proteins. See page 3, lines 23-25. A solution suspected of containing the kinases is applied to the Tat-Stimulatory Factor-bound substrate and the kinases are isolated and identified. See page 17, line 29 to page 18, line 4. There is no disclosure or teaching in Sharp that the Tat-Stimulatory Factor protein is associated with the substrate, effective to stimulate the association of viable cells with the substrate. The substrate-bound Tat-Stimulatory Factor protein is mainly used to bind the kinases, the natural binding partner

for Tat- Stimulatory Factor protein so that the kinases may be isolated, and the Tat-Stimulatory Factor protein is used as the substrate in such isolation. See page 17, line 29 to page 18, line 4. This isolation process is similar to isolation by successive fractionation not involving any substrate. See page 18, lines 1-4. Thus, Sharp, et al. is not concerned with association of viable cells with substrates, the subject matter of claim 41. Therefore, the invention of claim 41 is not a matter of obvious design choice of modifying Sharp, et al. Since there is no teaching or motivation in Sharp concerning the association of Tat protein growth factors for stimulating the association of viable cells with the substrate, Applicants respectfully submit that the rejection of claim 41 under 35 U.S.C. § 103(a) as being unpatentable over Sharp, et al. is traversed.

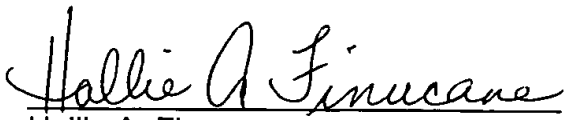
In view of the amendments and reasons provided above, it is believed that all pending claims are in condition for allowance. Applicants respectfully request favorable reconsideration, withdrawal of the rejections, and early allowance of all pending claims.

If a telephone conference would be helpful in resolving any issues concerning this communication, please contact Applicants' attorney of record, Hallie A. Finucane at (952) 253-4134.

Respectfully submitted,

Altera Law Group, LLC
Customer Number 22865

Date: August 1, 2003

By: 
Hallie A. Finucane
Reg. No. 33,172
HAF/mar